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# Identifying Chemical Hazards for Regulation: The Scientific Basis and Regulatory Scope of California's Proposition 65 List of Carcinogens and Reproductive Toxicants

William S. Pease\*

## Introduction

California's Proposition 65, the Safe Drinking Water and Toxic Enforcement Act of 1986,<sup>1</sup> has attracted considerable attention as an expression of "toxics populism" and as a model for innovative reform of chemical regulation. Reflecting widespread public concern that "current toxic laws aren't tough enough,"<sup>2</sup> the initiative statute established a new incentive structure for toxics regulation in an attempt to end the regulatory paralysis affecting conventional approaches to hazard identification, risk assessment and enforcement.<sup>3</sup>

Proposition 65 shifts the burden of proof in the regulatory process from government to industry. Use of chemicals known to cause cancer or reproductive toxicity is no longer considered "innocent" until proven "guilty" of harming public health by governmental agencies. Identified hazards are placed on a list and automatically become subject to the Act's warning requirements (12 months after listing) and discharge

\* Dr. Pease received his Ph.D. in Environmental Health Sciences from the University of California at Berkeley. He is an environmental planner with the San Francisco Bay Regional Water Control Board, CalEPA.

<sup>1</sup> CAL. HEALTH & SAFETY CODE (CH&SC) ch. 6.6, §§ 25249.5 et seq. (West 1986).

<sup>2</sup> I. REINER, *BALLOT ARGUMENT IN FAVOR OF PROPOSITION 65* (1986).

<sup>3</sup> Roe, *Incentive-Conscious Approach to Toxic Chemical Control*, 3 ECON. DEVEL. Q. 179-187 (1989).

prohibition (20 months after listing). Exemptions from these requirements are allowed only if the business responsible for an exposure or discharge can demonstrate that the amount of chemical in question poses “no significant risk.” Consequently, businesses have an economic incentive to avoid using listed chemicals or to keep exposures and discharges below levels that would pose any significant health risk. Both businesses and government also have a legal incentive to reach agreement quickly on the regulatory levels governing exemption from the law.

This paper focuses on Proposition 65’s approach to reforming the hazard identification component of traditional toxic chemical regulation. The environmental organizations promoting the initiative were concerned that no federal regulatory agency had taken action on more than one-third of the chemicals which had tested positive for carcinogenicity in National Toxicology Program bioassays.<sup>4</sup> Even less regulatory attention had been given to reproductive toxicants.<sup>5</sup> In an effort to forestall prolonged procedural debates over whether specific substances deserved regulation, Proposition 65 applies automatically to all substances that have been identified as carcinogens or reproductive toxicants by certain authoritative scientific or regulatory organizations. By requiring regulation once scientists reach consensus that a substance is a hazard, this approach immediately extends the scope of existing controls and ensures that the regulatory process does not lag behind scientific awareness of chemical hazards.

The “regulate upon identification” approach represents an effective means for increasing and accelerating the regulatory coverage of known hazards, but it also involves three major unforeseen consequences that deserve analysis before similar reforms of other environmental statutes are considered:

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<sup>4</sup> OFFICE OF TECHNOLOGY ASSESSMENT (OTA), IDENTIFYING AND REGULATING CARCINOGENS (1987).

<sup>5</sup> GENERAL ACCOUNTING OFFICE (GAO), REPRODUCTIVE AND DEVELOPMENTAL TOXICANTS: REGULATORY ACTIONS PROVIDE UNCERTAIN PROTECTION (1991).

First, the approach shifts the focus of political debate from establishing standards to identifying substances for regulation. Because only listed chemicals are affected by Proposition 65, hazard identification has become a principal arena of controversy between competing interest groups. Political concerns about regulatory impact have shaped the listing process and been interjected into scientific deliberations about a substance's toxicological characteristics, demonstrating how policy can influence science at even the hazard identification level of risk regulation.

Second, the approach requires that various regulatory and scientific organizations share a consensus about what constitutes sufficient evidence of hazard if a list that combines their identification efforts is to be consistent. Criteria for identification, however, can vary substantially across organizations. Substances will be evaluated differently depending on whether an organization is more concerned about preventing potential public health problems or minimizing the economic impact of false positive identifications. If a combined list reflects inconsistent criteria, regulatory resources may be misallocated as substances posing substantially different degrees of hazard are treated identically.

Third, the approach encourages judging regulatory performance by examining the extent of regulatory coverage rather than the effectiveness of regulatory controls. Proposition 65 emphasizes expanding its list of regulatory targets whenever there is scientific consensus that a substance is a carcinogen or reproductive toxicant. However, scientific considerations are not the only relevant criteria for selecting regulatory targets. An effective program must also consider whether there is significant human exposures to a substance and whether application of regulatory requirements is likely to reduce health risks. Extending regulatory coverage to more chemicals is attractive political symbolism, but there are no public health benefits and potentially significant administrative costs when targeted chemicals are neither in use nor susceptible to regulatory control.

This paper explores these issues by examining the origin, scientific basis and regulatory scope of the Proposition 65 list. As of January 1, 1992, the list included 376 carcinogens and 127 reproductive toxicants.<sup>6</sup> It represents the most extensive compilation of potential human carcinogens available from any state, national or international organization. Its list of reproductive toxicants is unique; no other organization has undertaken a generic hazard identification process for agents associated with male or female reproductive toxicity or developmental toxicity. The Proposition 65 list is becoming an authoritative source of hazard identification for a number of state and federal regulatory programs.<sup>7</sup>

Part II reviews the history of the list's expansion to reveal how the political context of Proposition 65 has influenced the use of scientific information in the regulatory process. Part III analyzes the selection criteria and evidence underlying the listing of chemicals to illustrate what tradeoffs are made between increasing the number of regulatory targets and ensuring that regulation is based on consistent evaluations of hazard. Part IV compares the uses of listed chemicals and their coverage under existing federal environmental statutes to provide a quantitative assessment of the regulatory scope of Proposition 65. The conclusion assesses the costs and benefits of Proposition 65's approach to reforming conventional hazard identification and identifies opportunities for improving the process of selecting targets for regulation.

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<sup>6</sup> Cal. Code of Regulations (CCR) tit. 22, § 12000 (1992).

<sup>7</sup> Pollution control laws which target chemicals identified as carcinogens or reproductive toxicants under Proposition 65 have been introduced in a variety of states. *See e.g.*, H. 4618, Massachusetts Act to Provide Warnings of Significant Health Risks from Toxic Chemicals (1990). Pending federal legislation to expand the universe of chemicals covered by emissions reporting requirements also incorporate the Proposition 65 list. *See e.g.*, H.R. 2880, The Community Right-to-Know More Act (1991).

### **The Origin and Expansion of the Proposition 65 List**

Confronted with the poor record of federal regulatory action on potential human carcinogens and reproductive toxicants, the proponents of Proposition 65 wanted to guarantee that scientifically identified hazards were automatically regulated. The law would apply to a list of agents “known to the State to cause cancer or reproductive toxicity” established by California’s Governor.<sup>8</sup> To redress the historical delays between hazard identification and regulation, this list was to include at a minimum substances already identified as carcinogens by the National Toxicology Program (NTP) and the International Agency for Research on Cancer (IARC) and as reproductive toxicants by the Occupational Safety and Health Administration (OSHA).<sup>9</sup>

To provide a scientific basis for additional listing decisions, California’s Governor is authorized to consult with the “State’s qualified experts,” who determine if “it has been clearly shown through scientifically valid testing according to generally accepted principles” that a chemical is a carcinogen or reproductive toxicant. To ensure that hazard identifications conducted by other groups were incorporated into the list, the State’s experts are authorized to designate regulatory agencies or scientific organizations they consider “authoritative” on carcinogenesis or reproductive toxicity. Chemicals identified by these bodies are automatically listed as known to the State to cause cancer or reproductive toxicity. In addition, substances that are “formally required... to be labeled or identified as causing cancer or reproductive toxicity” by other state or federal agencies are also automatically added to the Governor’s Proposition 65 list.<sup>10</sup>

With these four methods of listing (the minimum list, nomination by the State’s experts, identification by an authoritative body or by regulatory labeling requirements), proponents of Proposition 65

<sup>8</sup> CH&SC § 25249.8.

<sup>9</sup> CH&SC § 25249.8(a).

<sup>10</sup> CH&SC § 25249.8(b).

believed they had established an approach to hazard identification that would quickly increase the universe of chemicals affected by regulation. By emphasizing the role of scientific consensus in listing decisions (“authoritative” experts using “generally accepted principles”), environmentalists also hoped to preclude political considerations from this phase of the regulatory process. Listing decisions were exempted from the procedural constraints (like notice and comment requirements) typically applied to regulatory action.<sup>11</sup> Hazard identification was to take place separately from working out the regulatory implications of listing.

Since Proposition 65’s requirements apply automatically if a substance is listed, however, opponents of regulation are lead by the law’s structure to express their economic and political concerns during the hazard identification phase. Specific industries and businesses have attempted to prevent the listing of commercially important compounds and the regulated community in general has sought to restrict the scope of the law by slowing down the listing process. Delaying the initial date of listing is attractive because it postpones potentially costly compliance obligations.

During the first four years of Proposition 65 implementation, the regulated community possessed a strong ally in California’s Republican Governor, George Deukmejian, who had vigorously opposed the initiative statute.<sup>12</sup> Ignoring California voters’ determination that government agencies “have failed to provide them with adequate protection” against toxic chemicals,<sup>13</sup> the Deukmejian Administration

<sup>11</sup> CH&SC § 25249.8(e).

<sup>12</sup> The election of Republican Pete Wilson as Governor in 1990 may result in a new approach to implementing Proposition 65. The law’s incentive-based approach is compatible with the Wilson Administration’s interest in using market forces rather than conventional command and control regulation to achieve environmental goals. In addition, Proposition 65’s focus on reducing unnecessary exposures to toxic chemicals is consistent with the new Administration’s emphasis on preventing environmental and public health problems. P. WILSON, GOVERNOR’S REORGANIZATION PLAN NUMBER ONE: CREATING THE CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY (1991).

pursued an implementation strategy based on the premise that existing environmental regulations are generally adequate.<sup>14</sup> Believing that Proposition 65 “should not break new ground,”<sup>15</sup> the Administration sought to minimize the impact of the law in a variety of ways. In the area of hazard identification, the Administration attempted to restrict the number of chemicals affected by the law and to limit efforts to identify new carcinogens or reproductive toxicants that were not covered by existing regulations.

The creation of an administrative procedure for selecting, evaluating and ultimately listing chemicals as carcinogens or reproductive toxicants occurred within this political context. Proposition 65 includes several methods for identifying chemical hazards, but it was left to the Administration to define critical features of the listing process by regulation. A Scientific Advisory Panel (SAP) of the “State’s qualified experts” was created to advise the Governor on listing decisions<sup>16</sup> and

<sup>13</sup> CH&SC § 25249.5 (preamble).

<sup>14</sup> See W. Pease, *Environmental Pollution and Cancer in California: Evaluating the Significance of Risks under Proposition 65* (1988) (Masters Thesis, Energy and Resources Group, University of California at Berkeley), a detailed discussion of how State regulations issued to implement Proposition 65 generally maintain compliance with applicable federal laws (e.g., governing pesticide application, hazardous waste disposal or occupational hazard communication) constitutes compliance with Proposition 65.

<sup>15</sup> Statement by Thomas Warriner, Deputy Secretary of the California Health and Welfare Agency, *reported in* The Sacramento Bee, Oct. 23, 1988. Warriner was the Deukmejian Administration official responsible for implementing Proposition 65.

<sup>16</sup> While Proposition 65 authorizes the Governor to consult with “qualified experts” on listing decisions, CH&SC § 25249.8(d), it does not require formation of an advisory panel. The SAP was created by regulations, CCR §§ 12302-12305, which specified its composition and basic duties. The Governor retained complete control over the appointment and removal of Panel members and asserted his “discretion to accept or reject [Panel] advice in implementing the Act.” CALIFORNIA HEALTH AND WELFARE AGENCY (CHWA), FINAL STATEMENT OF REASONS, 22 CODE OF CALIFORNIA REGULATIONS DIVISION 2, SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT OF 1986 (1987).

The creation of scientific panels to advise regulatory agencies on controversial issues is a common practice, although the independence, representativeness and



to provide a forum for hazard identification debates. Announcing its formation, Governor Deukmejian maintained that hazard identification would not be politicized: "What we are doing is turning this decision over to the scientists, to the experts.... It won't be politicians making the decision. It won't be lobbyists for the business interest or lobbyists for environmental interests."<sup>17</sup>

The Deukmejian Administration, however, retained the ultimate authority to make listing decisions. It controlled both the membership and agenda of the SAP,<sup>18</sup> selecting which chemicals the Panel would evaluate. Through regulations, it specified the conditions under which hazard identifications made by authoritative bodies are automatically added to the Proposition 65 list.<sup>19</sup> Regulations also define how chemicals "formally required" to be labeled as carcinogens or reproductive toxicants by other agencies are identified.<sup>20</sup> The final say on listing decisions was delegated to the California Health and Welfare Agency (CHWA), the Governor's lead agency for implementing Proposition 65.<sup>21</sup> By shaping the listing process, the Administration could influence both the number and type of chemicals affected by Proposition 65's regulatory requirements.

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authority of such panels vary widely. S. JASANOFF, *THE FIFTH BRANCH: SCIENCE ADVISERS AS POLICYMAKERS* (1990). For one legal analyst's perspective on whether "Governor Deukmejian... actually stacked the Panel to promote his own political outlook," see Shaffer, *Improving California's Safe Drinking Water and Toxic Enforcement Act Scientific Advisory Panel Through Regulatory Reform*, 77 CAL. LAW REV. 1211-1258.

<sup>17</sup> Los Angeles Times, Mar. 13, 1987, at 30.

<sup>18</sup> K. Shaffer, *supra* note 16.

<sup>19</sup> CCR § 12306.

<sup>20</sup> CCR § 12902.

<sup>21</sup> Cal. Exec. Order D-61-87 (1987) (Gov. George Deukmejian). As a result of an administrative reorganization of environmental agencies in California, responsibility for Proposition 65 was shifted from the CHWA to a newly formed California Environmental Protection Agency in July 1991. Cal. Exec. Order W-15-91 (1991) (Gov. Pete Wilson).

*Delaying the Inevitable: How Identified Carcinogens  
Were not Initially Incorporated into the Proposition 65 List*

The first setback for environmentalist efforts to extend regulation to unaddressed hazards occurred February 27, 1987, when Governor Deukmejian announced that Proposition 65 applied to a short list of only 29 chemicals. This list included 26 substances with sufficient evidence of carcinogenicity in humans according to IARC or NTP and 3 chemicals identified by OSHA as reproductive toxicants. Ignoring the “minimum” list of more than 250 chemicals that was specifically referenced in the statute,<sup>22</sup> the CHWA maintained that the State was required to list only those chemicals known to cause cancer in humans, and not all chemicals known to cause cancer in experimental animals and hence suspected of being human carcinogens.

The Administration attempted to provide a scientific justification for its political decision to restrict the list, but it quickly became known that the CHWA had ignored the advice of its public health experts in the California Department of Health Services<sup>23</sup> (CDHS). Those experts argued unsuccessfully that the Governor was “scientifically and ethically” required to apply Proposition 65 to the larger list of animal carcinogens and emphasized that “from its perspective, the Department of Health Services does not believe human exposures to known animal carcinogens to be in the best interest of public health.”<sup>24</sup>

Environmentalists maintained that the Deukmejian Administration was placing special interests above human health. Al Meyerhoff, an attorney for the Natural Resources Defense Council, charged that chemical companies had influenced the Governor to shorten the list and accomplished “through the back door what they couldn’t do at the polls.”<sup>25</sup> Joining with labor unions, proponents of Proposition 65

<sup>22</sup> CH&SC § 25249.8(a).

<sup>23</sup> Los Angeles Times, Mar. 17, 1987, at 3.

<sup>24</sup> Memo from S. Book to Alex Kelter, Cal. Dept. of Health Services (Jan. 22, 1987) (discussing the use of animal carcinogens for the Proposition 65 list of cancer causing chemicals).

promptly filed suit to expand the list and won the first round in court. In April 1987, the Sacramento County Superior Court ordered the Governor to add more than 200 chemicals to his initial list.<sup>26</sup>

The Deukmejian Administration continued to resist the automatic extension of Proposition 65's requirements to all the substances identified as potential human carcinogens by IARC and NTP. Pursuing a very effective strategy of delay, the CHWA appealed the Court's decision and directed the Governor's SAP to evaluate all the disputed compounds from the "minimum" list substance-by-substance. The SAP obliged, reviewing the CHWA's "candidate" list of carcinogens alphabetically and slowly recommending that they be added to the Proposition 65 list.<sup>27</sup> Through its control over the SAP's agenda, the Administration ensured that the Panel spent its initial two years reviewing data on chemicals that were already legally covered by Proposition 65 rather than conducting de novo hazard identifications.

Throughout the political struggle over the size of the Proposition 65 list, the Governor's expert advisors on the SAP approached their tasks from a predominantly scientific perspective, questioning neither the Administration's control of their agenda nor the legal ramifications of their review of the "minimum" list. As scientists representing the different disciplines involved in cancer and reproductive risk assessment, SAP members clearly preferred conducting their own evaluations of toxicological data to simply accepting hazard

<sup>25</sup> Los Angeles Times, Feb. 28, 1987, at 1.

<sup>26</sup> AFL-CIO v. Deukmejian, No. 348195 (Sacramento County Superior Court April 24, 1987).

<sup>27</sup> Safe Drinking Water and Toxic Enforcement Act Scientific Advisory Panel (SAP) members invited efforts to prioritize their evaluations on the basis of a chemical's "inherently controversial nature, high public visibility.... [or potential for] widespread human exposure in California." SAP, TRANSCRIPT OF PUBLIC MEETING ON OCT. 30, 1987, at 11, 156 (Capitol Reporters 1987) (subsequent references to SAP transcripts are cited only as SAP — with date and page number). When no schemes to rank chemicals by opportunity for exposure or regulatory control were subsequently proposed, the SAP proceeded alphabetically except for its consideration of alcohol and tobacco.

identifications by other organizations. The SAP's predisposition to independent review facilitated the Administration's efforts to minimize the impact of Proposition 65 listing methods that had been designed to accelerate hazard identification.

By the time the Deukmejian Administration's position on the "short" list was finally repudiated by the courts, the environmentalist's legal victory actually had only a limited impact on the size of the Proposition 65 list. California's Court of Appeal upheld the lower court's order to expand the Proposition 65 list in July 1989, but by then about 90% of the chemicals at issue had already been nominated by the SAP and placed on the list. The Administration's strategy of delay had granted temporary regulatory reprieves of from 1 to 30 months for many chemicals, as well as monopolized the agenda of the SAP. While the Court emphasized that Proposition 65 directs the State and the SAP "to engage in a diligent, thorough, and continuing search for additional chemicals which evolving scientific knowledge demonstrates are subject to the Act,"<sup>28</sup> the Deukmejian Administration successfully frustrated new hazard identification efforts through its control over the listing process.

Environmentalists believed chemical-by-chemical reviews were unnecessary if substances had already been identified as carcinogens. One goal of Proposition 65 was to establish a listing process that automatically incorporated hazard identifications by other scientific and regulatory organizations. To initiate this process, the proponents of Proposition 65 petitioned the SAP to designate EPA and other agencies as "authoritative" bodies; chemicals identified by these agencies could then be added to the Governor's list without further review. Concerned about losing their prerogative to make listing decisions, the SAP decided not to recognize any authoritative bodies.<sup>29</sup>

To environmentalists, the SAP's refusal to designate authoritative

<sup>28</sup> AFL-CIO v. Deukmejian, 212 Cal. App. 3d 425, 440 (1989).

<sup>29</sup> SAP, Oct. 30, 1987, at 158.

bodies was just another manifestation of the Administration's strategy of delaying full implementation of Proposition 65.<sup>30</sup> They challenged the policy in court, charging the SAP with "arbitrarily failing to act" and "abuse of discretion," and won a summary judgment in April 1989.<sup>31</sup> Confronted with the Court's order to evaluate various organizations for designation as authoritative bodies, the SAP subsequently agreed to accept hazard identification decisions made by EPA,<sup>32</sup> IARC and NTP<sup>33</sup> and the Food and Drug Administration (FDA) and the National Institute of Occupational Safety and Health (NIOSH).<sup>34</sup>

Policy concerns about the potential regulatory impact of Proposition 65 have clearly shaped the role of independent scientific review in the listing process. In order to prevent Proposition 65 from applying immediately to hundreds of chemicals that had been identified as carcinogens by 1987, the Deukmejian Administration initially insisted that the SAP reevaluate each chemical individually. After the adverse court decisions of 1989, this policy shifted as the Administration sought to ensure its control over the listing process. Once it became inevitable that the Proposition 65 list would include virtually all the chemicals that have been identified as carcinogens by other authoritative agencies, further Administration efforts to restrain growth of the list focused on discouraging de novo hazard identification by the Panel.

CHWA informed the SAP in late 1989 that evaluating data on chemicals that were identified as carcinogens by other authoritative bodies was unnecessary.<sup>35</sup> Using its control over the SAP agenda, the

<sup>30</sup> San Francisco Chronicle, April 4, 1989, at 1.

<sup>31</sup> *AFL-CIO v. Deukmejian*, No. 359223 (Sacramento County Superior Court June 22, 1988).

<sup>32</sup> SAP, April 14, 1989.

<sup>33</sup> SAP, Oct. 20, 1989.

<sup>34</sup> SAP, April 6, 1990. The SAP declined to designate the American Council of Governmental and Industrial Hygienists as authoritative because the Panel was unfamiliar with the ACGIH identification process. California regulatory agencies were not designated as authoritative to avoid the appearance of conflict of interest; both CDHS and the California Department of Food and Agriculture (CDFA) are active in the regulatory implementation of Proposition 65.

Administration effectively eliminated further carcinogen identification efforts by the Panel. No resources were allocated to identifying chemicals that had bioassay data but remained unevaluated by other groups; panel discussions were redirected to risk assessment issues. While the Proposition 65 list has slowly grown to include the results of most existing carcinogen identification efforts, the listing method that environmentalists expected to make new contributions to hazard identification has proven to be a disappointment: The SAP has been responsible for identifying only one of 117 carcinogens listed between October 1989 and January 1992.<sup>36</sup>

### *Searching for Authority:*

#### *Bases for Identifying Reproductive Toxicants*

Proposition 65's mandate to regulate reproductive toxicants presents a significant challenge to conventional approaches to hazard identification. Reproductive endpoints like developmental toxicity and male or female reproductive toxicity have not been the focus of chemical testing programs and have rarely served as the basis for regulation.<sup>37</sup> In contrast to the situation with carcinogens, no scientific or regulatory agencies have compiled lists of known reproductive toxicants. With reproductive toxicants, the reform sought by the proponents of

<sup>35</sup> The CHWA informed SAP members that "if the Panel identifies EPA, IARC, and NTP as authoritative bodies for purposes of Proposition 65, there will be no need to discuss the chemicals" identified by these organizations as carcinogens. Letter from S. Book, CHWA, to SAP Members on Aug. 9, 1989.

<sup>36</sup> The SAP has reviewed data on only two potential carcinogens since mid-1989. It evaluated two pesticides at its April 1991 meeting, listing oxadiazon and refusing to list tetrachlorvinphos. Neither substance was considered as a result of de novo hazard identification efforts by the Panel. Oxadiazon had been deferred from an earlier meeting, where it was brought to the Panel's attention because it was on an EPA list of potential carcinogens. Tetrachlorvinphos had also been deferred from an earlier meeting, where it was brought to the Panel's attention because of National Cancer Institute test results.

<sup>37</sup> GENERAL ACCOUNTING OFFICE (GAO), REPRODUCTIVE AND DEVELOPMENTAL TOXICANTS: REGULATORY ACTIONS PROVIDE UNCERTAIN PROTECTION (1991).

Proposition 65 transcended establishing legal mechanisms for extending regulatory coverage automatically to hazards identified by other authorities. Success would require the creation of both a scientific consensus on how to define reproductive hazards and a review process that could systematically evaluate data and identify substances for listing.

Listing reproductive toxicants was initially a major focus of the SAP. With CDHS staff support, the SAP added ten chemicals to the Governor's initial list of three reproductive toxicants by July 1987, formed a Subpanel on Reproductive Toxicity and developed a priority list for future nominations.<sup>38</sup> The first compounds to be identified were either drugs (like diethylstilbestrol and thalidomide) or environmental contaminants (like methyl mercury) with extensive human evidence of reproductive harm.

The SAP's ability to reach agreement quickly on hazard identification decisions eroded once it finished reviewing data on textbook reproductive toxicants. To guide their assessment of substances with limited human evidence or just animal evidence, Panel members decided to "develop guidelines criteria used for identifying teratogens or reproductive toxicants."<sup>39</sup> The SAP had confronted a similar need for carcinogen identification guidelines, but it had decided to "recognize the work that's already been done in the field without reinventing it"<sup>40</sup> and use existing EPA guidelines. Apparently unaware that there were comparable EPA guidelines for reproductive hazard identification,<sup>41</sup> the SAP suspended listing activities and began

<sup>38</sup> SAP, April 14, 1988.

<sup>39</sup> SAP, Mar. 31, 1987, at 30.

<sup>40</sup> *Id.*, at 110.

<sup>41</sup> At the first SAP meeting, Chairman Kilgore reported that he was advised by the reproductive scientists on the Panel that "we do not have the guidelines that we have available for carcinogens." The full Panel's subsequent discussion makes no mention of the existence of EPA criteria for identifying developmental toxicants (published in 1986) or draft EPA criteria for identifying male and female reproductive toxicants. SAP, Mar. 31, 1987, at 118 et seq. EPA developmental criteria were briefly cited at

developing its own guidelines.

Shaping the criteria for listing became a major focus of all parties interested in the regulatory impact of Proposition 65.<sup>42</sup> The effort to initiate a generic process for identifying reproductive toxicants occurred in an even more politically charged context than carcinogen identification. While many listed carcinogens are already regulated under other environmental laws, identifying reproductive toxicants under Proposition 65 promised to subject a previously unaddressed class of toxic compounds to stringent new requirements. The law's proponents encouraged the SAP to adopt guidelines that were consistent with EPA's approach and quickly return to evaluating chemicals for listing.

Concerned that thousands of chemicals have at least some evidence of reproductive toxicity, opponents of Proposition 65 sought to delay reproductive hazard identification. They argued that the consequences of listing a substance under Proposition 65 would be so severe (*e.g.*, costly restrictions on chemical use, inappropriate public response to warnings) that novel constraints needed to be placed on established approaches to hazard identification. Represented by the International Life Sciences Institute-Nutrition Foundation (ILSI), a group which receives its support from food industry corporations, opponents maintained that current federal guidelines on reproductive toxicity needed to be significantly modified. ILSI's own "expert committees" proposed hazard identification criteria<sup>43</sup> which narrowly defined reproductive toxicity, restricted the types of evidence considered sufficient for listing and generally limited the number of chemicals likely to be affected by Proposition 65.<sup>44</sup>

the first Subpanel meeting devoted to guidelines development, SAP Subpanel, April 14, 1988, at 62, but there appears to have been no discussion of simply adopting these criteria.

<sup>42</sup> Pease, *When Scientists Become Policy Makers: Shaping Hazard Identification under Proposition 65*, 5 REPROD. TOXICOL. 169-173 (1991).

<sup>43</sup> Mattison et al., *Criteria for Identifying and Listing Substances Known to Cause Developmental Toxicity under California's Proposition 65*, 4 REPROD. TOXICOL. 163-175 (1990).



In such a contested debate, the Reproductive Subpanel's effort to develop its own approach to reproductive hazard identification collapsed as it sought to base its policy decisions on existing scientific consensus. It ultimately proposed criteria for identifying developmental toxicants<sup>45</sup> that were substantially equivalent to existing EPA guidelines.<sup>46</sup> Plans to develop independent criteria for identifying male and female reproductive toxicants never materialized; the SAP criteria incorporate EPA female and male reproductive toxicity guidelines by reference.<sup>47</sup>

Completion of the developmental toxicity guidelines in late 1988 appeared to provide the SAP with the evaluation criteria it needed to address more difficult listing decisions. Only two substances had been listed during the period of guidelines development; both had substantial human evidence of reproductive toxicity (ethyl alcohol in alcoholic beverages and tobacco smoke). During 1989, the SAP identified 16 reproductive toxicants, including several industrial chemicals with strong animal evidence but only limited human data (*e.g.*, glycol ethers).

This renewed listing activity was short-lived, however. As with carcinogens, the Deukmejian Administration used its administrative control over the listing process to discourage *de novo* hazard identification by the SAP and ensure that new listings did not extend regulatory controls to unaddressed chemicals. The Reproductive Subpanel that had been screening reproductive toxicants for the full SAP was allowed to disintegrate by the CHWA.<sup>48</sup> With no members who

<sup>44</sup> Pease, *supra* note 42.

<sup>45</sup> SAP, CRITERIA FOR RECOMMENDING CHEMICALS FOR LISTING AS "KNOWN TO THE STATE TO CAUSE REPRODUCTIVE TOXICITY" (1988).

<sup>46</sup> Environmental Protection Agency (EPA), Proposed Amendments to the Guidelines for the Health Assessment of Suspect Developmental Toxicants, 53 Fed. Reg. 9386-9403 (1989).

<sup>47</sup> EPA, Proposed Guidelines for Assessing Female Reproductive Risk, 53 Fed. Reg. 24834-24847 (1988); EPA, Proposed Guidelines for Assessing Male Reproductive Risk, 53 Fed. Reg. 24850-24868 (1988).

<sup>48</sup> After the Subpanel's February 1989 meeting, its initial four members resigned because of other professional commitments or frustration with the Proposition 65

participated in creating the consensus on hazard identification guidelines and only one expert in reproductive toxicity, the full SAP now has only a limited institutional capacity to identify reproductive hazards. The SAP has been responsible for identifying only four of the 99 reproductive toxicants listed between October 1989 and January 1992.<sup>49</sup>

The CHWA has largely taken over the listing process, acting to restrict listing to those substances already regulated by other federal regulatory agencies as reproductive toxicants. Unwilling to allow the SAP to make major new contributions to reproductive hazard identification, the Administration has sought out other "authoritative" sources for listing. It has relied most heavily on labeling requirements established by FDA for prescription drugs, almost doubling the Proposition 65 list of reproductive toxicants during 1990.<sup>50</sup> As with recently identified carcinogens, these listings have occurred automatically, without any review by the SAP or reference to the SAP guidelines. Because federal drug regulation is generally more stringent than Proposition 65 (and preempts state regulation as well), listed prescription drugs are generally unaffected by Proposition 65's regulatory requirements. By focusing on listing drugs, the Deukmejian Administration was able to appear as if it was extending Proposition 65's coverage of reproductive toxicants without actually imposing any new regulatory burdens on commercial interests.

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process and were never replaced by the CHWA.

<sup>49</sup> The SAP has reviewed data on five reproductive toxicants since mid-1989 and decided to list aspirin, PCBs, toluene and benomyl.

<sup>50</sup> After the CHWA began placing therapeutic drugs on the SAP agenda in 1989, Panel member Diana Petitti recommended designating FDA as an authoritative body in order to preclude time-consuming, case-by-case reviews and to devote resources to evaluating chemicals other than drugs. Letter to S. Book, CHWA (Nov. 30, 1989). While the SAP subsequently designated FDA as authoritative in April 1990, CHWA chose not to list FDA-rated drugs as reproductive toxicants under the authoritative bodies rule, relying instead on the regulatory labeling rule that did not require any sufficiency of evidence test. See note 94 *infra* for a complete discussion of the CHWA focus on listing drugs.

### *Controlling Hazard Identification:*

#### *The Administrative Implementation of Environmental Reform*

Proposition 65's "regulate upon identification" approach has not eliminated the concerns about economic and political impact that have traditionally paralyzed toxic chemical regulation. The State's approach to listing substances under Proposition 65 has been primarily determined by concerns about regulatory impact rather than by commitment to improving the hazard identification process. During the Deukmejian Administration's implementation of the law, one principal Proposition 65 reform (automatic extension of regulatory coverage to known toxicants) was successfully delayed and another (establishment of an independent chemical review process) was completely frustrated. The law's explicit mandate to list carcinogens already identified by authoritative organizations was ignored by the Deukmejian Administration. Over two years were required to extend Proposition 65's regulatory requirements to the chemicals on its initial "minimum" list.

While political opposition to accelerating regulatory coverage of known hazards was eventually overcome, it has proven more difficult to create an institutionalized source of de novo hazard identification. No independent process for reviewing toxicological data and identifying new hazards has been established. Using its control of the SAP's agenda and resources, the Deukmejian Administration virtually eliminated the Panel's role in the Proposition 65 listing process.<sup>51</sup> The SAP has considered listing only two carcinogens and five reproductive toxicants since October 1989. Figure 1 shows the number of chemicals evaluated for carcinogenicity and reproductive toxicity at each SAP meeting since June 1987, revealing the dramatic decline over time of the

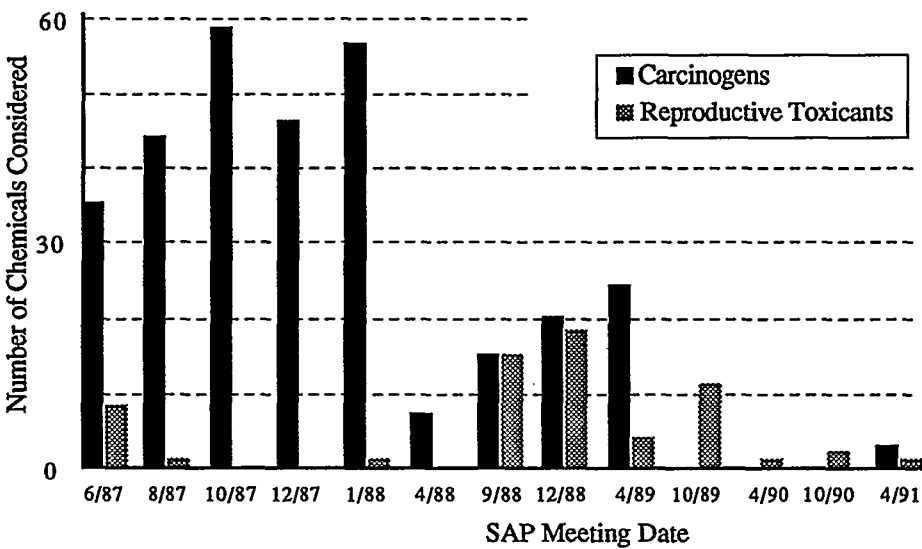
<sup>51</sup> In 1989, the CHWA reduced the SAP schedule to two meetings per year instead of four and directed the SAP to review quantitative risk assessments of listed Proposition 65 chemicals. As a result of political changes at the gubernatorial level in California, the SAP has not met for any purpose since April 1991.

Panel's hazard identification efforts.

The State's administrative control over the Proposition 65 listing process has had a much more substantial impact on the law's effort to extend regulatory controls to reproductive toxicants than carcinogens. While the listing of many carcinogens may have been delayed, it could not be completely prevented. For reproductive toxicants, the absence of other authoritative hazard identification programs allowed the State considerably more opportunity to limit Proposition 65's impact. By preventing the creation of an independent chemical review process, the State ensured that the law's goal of instituting the first generic regulatory program focused on reproductive toxicants would remain unfulfilled.

**Figure 1**

**Number of Chemicals Evaluated at SAP Meetings**



### Scientific Consistency of the Proposition 65 List

The listing methods established by Proposition 65 intentionally combine hazard identification efforts by various regulatory and scientific organizations, but the law establishes no mechanism for ensuring that listing decisions are supported by consistent evidence. Proposition 65 requires that SAP nominated chemicals be “clearly shown through scientifically valid testing according to generally accepted principles to cause cancer or reproductive toxicity,”<sup>52</sup> but provides no additional guidance on how strong evidence needs to be for listing. The statute establishes no explicit requirements for chemicals listed as a result of identification by authoritative bodies or regulatory labeling.<sup>53</sup> Aiming to compile a list of regulatory targets quickly, proponents of the law avoided attempting to define the amount of scientific evidence required to justify preventive regulation.

The absence of guidance about what constitutes sufficient evidence for listing has two potentially adverse consequences for the Proposition 65 hazard identification process. First, to the extent that the combined list reflects inconsistent criteria, regulatory resources may be misallocated as substances posing substantially different degrees of hazard are treated identically. Second, opportunities to introduce a double standard into listing decisions have increased. The evidentiary threshold for listing commercially significant substances can be higher than for unimportant substances. This section assesses the consistency of evidence used to support listing by examining how substances were identified as hazards. Methods of listing and sources for identification<sup>54</sup> of carcinogens and reproductive toxicants are reviewed.

<sup>52</sup> CH&SC § 25249.8(b).

<sup>53</sup> Interpreting the ambiguous language of Proposition 65, CHWA regulations have further confused this issue by imposing a sufficiency of evidence test on identifications by authoritative bodies, CCR § 12306, but not on identifications by regulatory labeling requirements. In the case of listing as a result of labeling, substances are known to cause cancer or reproductive toxicity if a formally required message is “intended to communicate a risk” of cancer or reproductive toxicity, no matter what strength of evidence supports the warning. CCR § 12902.

<sup>54</sup> CHWA, CHEMICALS KNOWN TO THE STATE TO CAUSE CANCER OR REPRODUCTIVE

### Carcinogens

Table 1 classifies listed Proposition 65 carcinogens by their method of listing and by the agency responsible for their identification as carcinogens. As a result of independent efforts, the SAP has identified 54 chemicals as carcinogens.<sup>55</sup> If one accepts the legal decision that a "minimum" list of 235 carcinogens was established by Proposition 65, it is clear that the vast majority (85%) of carcinogens have been listed on the basis of hazard identifications made by two authoritative scientific organizations, NTP and IARC. Several regulatory agencies have also made contributions as authoritative bodies: EPA, for example, is responsible for identifying most pesticides listed as carcinogens. Very few chemicals have been listed as carcinogens on the basis of regulatory labeling requirements.<sup>56</sup>

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#### TOXICITY: BASIS FOR LISTING (1991).

<sup>55</sup> Crediting the SAP for their review of agents on the "minimum" list increases their hazard identification contribution from 15% to almost 60% of the list. Assuming that 43 of the 54 agents listed as a result of SAP de novo review would have eventually been listed automatically because they had been classified by an authoritative body reduces the SAP's contribution to less than 5% of the list.

<sup>56</sup> Warning requirements for occupational carcinogens have been used inconsistently as a source of listing by the CHWA. Five chemicals labeled "cancer hazard" or "regulated carcinogen" by California OSHA were automatically listed in July 1987, SAP, June 18, 1987, at 6 et seq. & 162 et seq., while eight chemicals labeled "cancer suspect agent" (a term applied by OSHA to several known human carcinogens) and one labeled "potential cancer hazard" were not listed on the basis of warning requirements. CCR tit. 8, §§ 5209-5220.

**Table 1**  
**Method of Hazard Identification: Carcinogens**

<i>Method of Listing</i>	<i>Total<sup>57</sup></i>	<i>Source of Hazard Identification</i>					
		<i>IARC</i>	<i>NTP</i>	<i>EPA</i>	<i>FDA</i>	<i>NIOSH</i>	<i>OSHA</i>
<i>Agents on Minimum List</i>	<i>235</i>	<i>205</i>	<i>162</i>				<i>8</i>
Governor's initial list	27						
SAP review	176						
Labeling requirement	5						
Duke I lawsuit <sup>58</sup>	28						
<i>Agents not on Min. List</i>	<i>141</i>	<i>62</i>	<i>25</i>	<i>55</i>	<i>5</i>	<i>5</i>	<i>0</i>
Authoritative body	86	43	12	29	4	5	NA <sup>59</sup>
Labeling requirement	1						
SAP de novo reviews	54						
• Agents not classified as carcinogens by IARC, EPA or NTP	11						
• Agents classified <sup>60</sup> as carcinogens by IARC, EPA or NTP	43	19	13	26			
<b><i>Total</i></b>	<b><i>376</i></b>	<b><i>267</i></b>	<b><i>187</i></b>	<b><i>55</i></b>	<b><i>5</i></b>	<b><i>5</i></b>	<b><i>8</i></b>

<sup>57</sup> In all tables, the sums exceed subtotals because of overlaps in subcategories. Here, for example, several organizations have identified the same listed agent as a carcinogen.

<sup>58</sup> The case in which environmentalists challenged the State's initial short list of Proposition 65 compounds is known as "Duke I." After the California Court of Appeals ruled against the State, 28 substances on the minimum list that had not yet been reviewed by the SAP were automatically listed.

<sup>59</sup> OSHA is not an "authoritative body."

<sup>60</sup> The SAP evaluated a number of agents that were classified as carcinogens by various agencies before it designated those agencies as authoritative bodies. Agents classified by an authoritative body (e.g., EPA B2 carcinogens) and possessing sufficient evidence of carcinogenicity (according to CCR § 1306) would have eventually been listed automatically.

Concerns about creating a list of carcinogens without consistent hazard identification criteria were taken into account early in the listing process. The SAP decided to rely on existing EPA carcinogen identification guidelines in its evaluations.<sup>61</sup> To address SAP concerns about the adequacy of chemical evaluations conducted by authoritative bodies like NTP and IARC, the CHWA issued regulations requiring that their hazard identifications meet defined criteria for “sufficient evidence” in order for a chemical to be automatically listed.<sup>62</sup> While there are differences between NTP’s approach, IARC’s strength of evidence approach and EPA’s weight of evidence approach,<sup>63</sup> these authoritative bodies share common definitions of what constitutes sufficient evidence for identifying a chemical as a potential human carcinogen.<sup>64</sup>

Application of uniform identification criteria has created a list of chemicals supported by relatively consistent evidence of carcinogenicity. Chemicals identified by authoritative bodies using substantially different criteria than EPA have been subjected to more intensive review by the CHWA before automatic listing. FDA, for example, relies on expert committees working without uniform guidelines to identify carcinogens. It has accepted single positive bioassays as evidence of carcinogenicity and rarely publishes its identification decisions. After CHWA review, only a portion of chemicals considered carcinogens by FDA have been

<sup>61</sup> SAP, Mar. 31, 1987, at 109; SAP, June 18, 1987, at 64.

<sup>62</sup> CCR § 12306.

<sup>63</sup> Ashby et al., *A Scheme for Classifying Carcinogens*, 12 REGUL. TOXICOL. PHARMACOL. 270-295 (1990).

<sup>64</sup> Matula & Somers, *The Classification of Chemical Carcinogens*, 10 REGUL. TOXICOL. PHARMACOL. 174-182 (1989). The few disagreements over hazard identification between the SAP, EPA, NTP and IARC have been limited to chemicals with marginal carcinogen rankings. While the SAP generally considers EPA Category C or IARC Group 3 compounds to have insufficient evidence of carcinogenicity, its independent review of the data has led to the listing of several such chemicals. Two chemicals that elicited extensive discussions before listing were para-dichlorobenzene, SAP, Dec. 16, 1988, at 100 et seq., and oxadiazon, SAP, April 26, 1991, at 5 et seq.



listed.<sup>65</sup> Similarly, a number of commercially important agents considered potential occupational carcinogens by NIOSH (e.g., asphalt fumes) have not been listed automatically because of problems with formal documentation or evidence.<sup>66</sup>

The State's effort to ensure that listed carcinogens meet its criteria for sufficient scientific evidence has involved a significant tradeoff between scientific consistency and extent of regulatory coverage. Because Proposition 65 establishes no evidentiary test for substances identified as a result of labeling requirements, a large number of chemicals regulated in the workplace have potential for listing. OSHA's Hazard Communication Standard requires that industry provide workers with warnings on material safety data sheets about all substances which have exhibited carcinogenic potential in one valid, positive animal bioassay.<sup>67</sup> Although these substances satisfy Proposition 65's procedural criteria for automatic listing, many do not meet the State's sufficiency of evidence test. Consistent with its policy of restricting the extent of Proposition 65's coverage, CHWA has used its administrative discretion to avoid listing so many potential occupational carcinogens.

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<sup>65</sup> In 1990, CDHS identified a set of 38 chemicals considered carcinogens by FDA, but the lack of public documentation and/or the failure to meet criteria for sufficiency of evidence, CCR § 12306, resulted in only 7 compounds being listed authoritatively.

<sup>66</sup> In 1990, CDHS identified a set of 28 agents considered potential occupational carcinogens by NIOSH, but the lack of public documentation and/or the failure to meet criteria for sufficiency of evidence, CCR § 12306, resulted in only 5 compounds being listed authoritatively. NIOSH also identifies several classes of compounds (monohalomethanes and vinyl halides) as potential occupational carcinogens, National Institute for Occupational Safety and Health (NIOSH), *NIOSH Recommendations for Occupational Safety and Health Standards*, 37(S-7) MMWR SUPPLEMENT 1-29 (1988), but CHWA has not listed specific chemicals like methyl bromide, methyl chloride or vinyl fluoride because they do not individually meet sufficiency of evidence criteria.

<sup>67</sup> 29 C.F.R. §§ 1910 & 1200 (1990).

*Reproductive Toxicants*<sup>68</sup>

Table 2 classifies listed Proposition 65 reproductive toxicants by their method of listing and by the agency responsible for their identification as hazards. Independent review by the SAP has identified 27% of listed reproductive toxicants, double the Panel's de novo contribution to carcinogen identification. The Panel has played a more important role because no scientific or regulatory agencies have organized programs to identify reproductive toxicants. Just two reproductive toxicants have been listed as a result of identification by authoritative bodies: TCDD (by EPA) and nitrofurantoin (by NTP).

In contrast with carcinogens, most reproductive toxicants (72%) have been listed automatically on the basis of regulatory labeling requirements. FDA prescription drug labels account for 65% of the list; EPA and CDFA pesticide labels account for 7% of the list.<sup>69</sup> Among

<sup>68</sup> The CHWA officially lists reproductive toxicants as male, female or developmental toxicants, although this classification is not based on recommendations made by the SAP or any complete review of available toxicological data. The SAP Reproductive Subpanel regularly recommended listing chemicals as "reproductive toxicants," without specifying the type of toxicity. The basis for the State's classification of reproductive endpoints was questioned publicly during an SAP Subpanel meeting (using the example of ethylene oxide), but CHWA never provided an adequate explanation of its approach. SAP Subpanel, Oct. 31, 1988, at 79 et seq.

Classification generally indicates which reproductive endpoint possessed the strongest evidence of toxicity, but it cannot be reliably used to distinguish which populations are susceptible to listed compounds. Ethylene oxide, for example, was listed as a female reproductive toxicant on the basis of OSHA regulation. There is, however, both suggestive evidence in human males and clear evidence in rats and monkeys that the chemical is a male reproductive toxicant as well. AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY (ATSDR), TOXICOLOGICAL PROFILE FOR ETHYLENE OXIDE (1990). There are several examples where SAP members stated compounds were "reviewed only for developmental toxicity" and agreed that they also possessed evidence of male reproductive toxicity, but CHWA only listed them as developmental toxicants (e.g., chlorambucil, SAP Subpanel, Oct. 31, 1988, at 123). Similar inconsistencies are apparent in the classification of listed therapeutic drugs: label warnings for procarbazine hydrochloride, for example, note case reports of developmental toxicity and clinical studies indicating azoospermia and antifertility effects, PHYSICIAN'S DESK REFERENCE (PDR) (1991), but the drug is only listed as a developmental toxicant.

scientific and regulatory agencies, FDA has played the predominant role in reproductive hazard identification because it has the statutory authority to require that pharmaceutical manufacturers report adverse effects from use of their products. The strongest evidence of reproductive toxicity generally involves epidemiological studies of human high dose exposures, but such exposures are regularly monitored only in therapeutic settings. Since there is no mandatory surveillance of high dose exposures occurring in the workplace, there is usually less human evidence of reproductive toxicity for commercial chemicals.

**Table 2**  
**Method of Hazard Identification: Reproductive Toxicants**

<i>Method of Listing</i>	<i>Total</i>	<i>Source of Hazard Identification</i>					
		<i>FDA</i>	<i>NTP</i>	<i>EPA</i>	<i>CDFA</i>	<i>Calif.</i>	<i>OSHA</i>
Governor's Initial List	3						3
Labeling requirement	91	82		6	3	1	
Authoritative Body	2		1	1			
SAP de novo review	31						
• Agents not classified by FDA	22						
• Agents classified by FDA	9						
<b>Total</b>	<b>127</b>	<b>82</b>	<b>1</b>	<b>7</b>	<b>3</b>	<b>1</b>	<b>3</b>

<sup>69</sup> As with carcinogens (*see supra* note 56), occupational warning requirements have been used inconsistently by the CHWA to identify reproductive toxicants. The California OSHA label for ethylene dibromide (EDB), for example, uses the same words ("may cause sterility") as the label for the listed male reproductive toxicant dibromochloropropane, CCR tit. 8, §§ 5212 & 5219, but EDB has never even been considered for listing as a reproductive toxicant.

Listing decisions made by the SAP or on the basis of EPA labeling have generally been supported by consistent evidence because of the similarity between SAP and EPA guidelines for evaluating developmental, male and female reproductive toxicants.<sup>70</sup> Listing decisions based on FDA labeling, however, are frequently not supported by similar types of evidence.<sup>71</sup> Compared with the SAP or EPA, FDA conducts hazard identification using a lower evidentiary threshold and a different process. No uniform criteria guide FDA efforts to identify reproductive toxicants (Frankos, 1985).<sup>72</sup> Suggestive case reports or chemical similarity may be sufficient to justify providing patients and physicians with a warning about potential adverse reproductive effects. The agency also considers tradeoffs which are unique to therapeutic agents, placing drugs in pregnancy categories based on the degree of risk to the fetus balanced against the drug's potential benefits to a patient.<sup>73</sup>

<sup>70</sup> The pesticide cyanazine may be an exception to this generalization. While listed as a result of EPA labeling requirements, its supporting evidence may not satisfy SAP criteria for identifying developmental toxicants. The birth defects associated with cyanazine are present "at doses which cause serious maternal illness in laboratory animals;" SAP criteria require special evaluations of this type of adverse effect.

<sup>71</sup> There is a wide range in the strength of evidence supporting FDA rating and labeling requirements. PDR (1991). This evidence includes well-conducted epidemiological studies (e.g., androgens and estrogens), case reports alone (e.g., procarbazine hydrochloride), reports of experience with a class of drugs (e.g., anti-convulsants and benzodiazepines), or very limited animal studies (e.g., mitomycin and clomiphene citrate). Some labeled drugs do not even have individual evidence of developmental toxicity. For example, there are no positive clinical reports or animal evidence to support identifying most aminoglycosides as developmental toxicants. FDA Category D ratings for these drugs are based only on their chemical similarity to streptomycin, which is associated with fetal deafness if used during pregnancy.

<sup>72</sup> Frankos, *FDA Perspectives on the Use of Teratology Data for Human Risk Assessment*, 5 FUND. APPL. TOXICOL. 615-625 (1985). FDA attempts to develop criteria to support consistent interpretation and use of reproductive data, Interagency Regulatory Liaison Group (IRLG), *Interagency Regulatory Liaison Group Workshop on Reproductive Toxicity Risk Assessment*, 66 ENVIRON. HEALTH PERSPECT. 193-221. (1986), were never completed.

By emphasizing hazard identification based on FDA drug labeling,<sup>74</sup> the Deukmejian Administration introduced a clear double standard into the Proposition 65 list of reproductive toxicants. Therapeutic drugs (which are unlikely to be affected by the law's regulatory requirements) have been listed on the basis of limited animal studies or even membership in a chemical class. Commercially significant substances, however, have only been listed if SAP or EPA sufficiency of evidence criteria are met. Ironically, the lower threshold of evidence for drugs originates in the FDA's health-conservative approach to identifying potential reproductive toxicants. If the State were to consistently apply such a preventive bias to the implementation of Proposition 65, a significant number of industrial substances would be suitable for listing. Many commercially significant substances that have been reviewed possess evidence of reproductive toxicity that is comparable to that supporting the listing of many therapeutic drugs.<sup>75</sup>

### **Regulatory Scope of the Proposition 65 List**

Proposition 65's proponents accepted that the law could "not cover all potentially harmful chemicals. It concentrates only on the known worst offenders."<sup>76</sup> The law's principal criterion for selecting

<sup>73</sup> 21 C.F.R. § 201.57 (1990). Current pregnancy category labeling for therapeutic drugs can be found in the PDR (1991).

<sup>74</sup> To obtain complete control over the listing of labeled reproductive toxicants, CHWA eliminated any review of its decisions by the SAP or even CDHS professional staff. Consequently, apparent agency errors in the use of FDA pregnancy categories, PDR (1991), were not corrected. CHWA failed to consistently list all drugs rated Category D ("positive evidence of human fetal risk or... known teratogenic effect in some animal species") or Category X ("studies in animals or human beings have demonstrated fetal abnormalities....contraindicated in women who are or may become pregnant"). For example, quinine is rated Category X with reports of congenital malformations in humans and strong evidence of teratogenicity in animals, but has not been listed. Five aminoglycosides are rated Category D and have identical supporting evidence, but only three have been identified as reproductive toxicants under Proposition 65. (Amikacin sulfate, netilmycin sulfate and tobramycin sulfate have been listed; kanomycin sulfate and neomycin sulfate have not.)

<sup>75</sup> J. SCHARDEIN, CHEMICALLY INDUCED BIRTH DEFECTS (1985).

regulatory targets is whether there is a scientific consensus that a substance is a carcinogen or reproductive toxicant. By creating a science-based list, environmentalists hoped to eliminate political considerations about regulatory impact from hazard identification debates. However, many substances with sufficient scientific evidence of carcinogenicity or reproductive toxicity may not be suitable targets for a regulatory program. Targeting substances which are not in commercial use or which are not amenable to applicable controls may waste regulatory resources. In addition to the strength of toxicological evidence, at least two criteria are relevant to the identification of "known worst offenders" for a regulatory program: a substance's potential for human exposure and its susceptibility to regulatory control.

To examine whether Proposition 65's science-based approach has generated a suitable list of regulatory targets, this section categorizes carcinogens and reproductive toxicants by their type of use<sup>76</sup> and by the extent to which they are covered by existing federal pollution control regulation.<sup>78</sup> In the absence of data on the volume of use or on the extent of public exposure for the majority of listed substances,<sup>79</sup> the

<sup>76</sup> YES ON 65, QUESTIONS AND ANSWERS ABOUT PROPOSITION 65 (1986).

<sup>77</sup> Chemical uses for listed compounds were ascertained from a review of IARC and NTP supporting documentation and the Merck Index (1989). Many listed compounds have more than one use, so chemical class totals exceed 100%. A spreadsheet of listed Proposition 65 carcinogens and reproductive toxicants specifying chemical uses and regulatory coverage is available from the author on request.

<sup>78</sup> Regulatory coverage was ascertained by cross-correlating the Proposition 65 list with the lists of chemicals affected by the following statutes: CAA: Clean Air Act, § 112 (list of hazardous air pollutants) CWA: Clean Water Act, § 304 (list of priority pollutants) SDWA: Safe Drinking Water Act, § 300 (list of substances with current or proposed national primary drinking water regulations) OSHA: Occupational Safety and Health Act, § 6 (list of substances with permissible exposure limits) RCRA: Resource Conservation and Recovery Act, Subtitle C (list of hazardous waste constituents) SARA: Superfund Amendments and Reauthorization Act, § 313 (list of substances subject to information disclosure requirements).

<sup>79</sup> See Pease et al., *Regulating Carcinogens under California's Proposition 65*, 10 RISK ANAL. 255-271 (1990) for a presentation of available exposure data on the most well-studied Proposition 65 carcinogens. The SARA Toxic Release Inventory, which provides data on chemical emissions but not on exposure, includes only 30%

type of chemical use serves as the best available indicator of potential exposure. Federal regulatory coverage of classes of listed substances is then examined to assess whether Proposition 65 has extended controls to previously unaddressed but commercially significant compounds.

### *Carcinogens*

Three hundred and seventy-six agents are listed as carcinogens under Proposition 65. Table 3 classifies these into broad categories of chemical use. The Proposition 65 list of carcinogens represents a reasonably broad sample from the universe of chemicals. Two-fifths (43%) of listed carcinogens are industrial substances; most are chemical intermediates used in manufacturing although some are present in final consumer products. Therapeutic drugs and food constituents each comprise an additional fifth of the list. Twenty-two percent of listed agents are prescription drugs, particularly anti-neoplastic agents. Eighteen percent are compounds that occur in food; about half of these are naturally occurring or the result of preparation and half are synthetic additives or environmental contaminants. Fifteen percent of listed chemicals are agricultural chemicals, primarily pesticides. Ten percent are energy-related substances, primarily combustion by-products, and 10% are laboratory research compounds. An additional 10% are chemicals associated with various life style choices, particularly smoking tobacco, drinking alcohol or using cosmetics. Two percent of listed compounds are associated with the use of chlorine as a disinfectant in water supplies or bleaching agent in industry.

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of the 500 carcinogens and reproductive toxicants listed under Proposition 65. About 40% of listed carcinogens and 90% of listed reproductive toxicants are not covered.

**Table 3**  
**Types of Use of Listed Proposition 65 Compounds**

<i>Type of Use</i>	<i>Carcinogens</i>	<i>Reproductive Toxicants</i>
<i>Industrial Substances</i>	$\Sigma = 161$ [43%]	$\Sigma = 12$ [9%]
Dyes or dye intermediates	51	0
Inorganics	14	2
Solvents	20	5
Others used or produced in mfg.	100	6
Present in consumer products	14	4
<i>Agricultural Chemicals</i>	$\Sigma = 56$ [15%]	$\Sigma = 15$ [12%]
Fungicide	16	7
Herbicide	7	3
Insecticide (pesticide)	28	8
Nematocide	5	1
Growth regulator	2	1
<i>Energy-Related Substances</i>	$\Sigma = 39$ [10%]	$\Sigma = 4$ [3%]
Fuel	6	0
Combustion by-products	29	3
Fuel additives	4	1
<i>Chlorination By-Products</i>	6 [2%]	1 [1%]
<i>Laboratory Research Compounds</i>	37 [10%]	0
<i>Food Constituents</i>	$\Sigma = 66$ [18%]	$\Sigma = 7$ [6%]
Natural	6	0
Mycotoxins	4	0
Preparation-related	20	0
Synthetic additives	16	0
Environmental contaminants	20	7
<i>Medicines</i>	$\Sigma = 81$ [22%]	$\Sigma = 102$ [80%]
Prescription drugs	79	100
Over-the-counter drugs	2	2
<i>Life Style Associated</i>	$\Sigma = 38$ [10%]	$\Sigma = 7$ [6%]
Tobacco-related	25	3
Alcohol-related	5	1
Other drugs	0	3
Cosmetics	10	0
<i>Radionuclides (as a class)</i>	1 [0%]	0



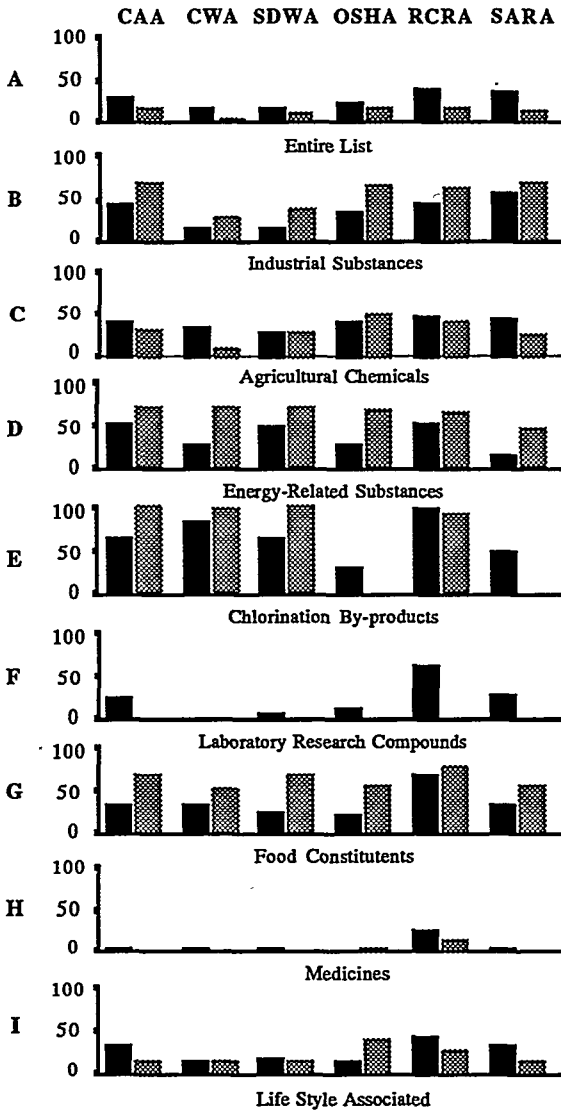
Figure 2 indicates the percentage of listed carcinogens that are covered by federal programs focused on controlling the quality of air, water, land or the workplace. In general, identified carcinogens appear to be underregulated: the vast majority of listed carcinogens are not covered under existing statutes (Figure 2(a)).<sup>80</sup> The extent of coverage increases if one examines the chemical use classes which are targeted by conventional regulatory programs. Coverage under most statutes increases for carcinogenic industrial substances (Figure 2(b)), agricultural chemicals (Figure 2(c)), energy-related substances (Figure 2(d)) and chlorination by-products (Figure 2(e)). Carcinogens that are outside the traditional purview of environmental agencies, like laboratory research compounds (Figure 2(f)), medicines (Figure 2(h)) and substances associated with life style choices (Figure 2(i)) are less frequently addressed.<sup>81</sup>

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<sup>80</sup> The distribution of coverage under different statutes illustrates that there is an inverse relationship between the scope of regulatory coverage and the stringency of regulatory requirements. Pease, *The Role of Cancer Risk in the Regulation of Industrial Pollution*, RISK ANAL. (in press). The largest percentages (35-45%) of identified carcinogens are affected by the least stringent requirements, such as information disclosure or handling rules. Smaller percentages (25% or less) are covered by standards limiting potential human exposure in the workplace or through other environmental media.

<sup>81</sup> Food constituents, which are not a principal target of the statutes examined in this analysis, are covered extensively (Figure 2(g)) because of the large proportion of n-nitroso compounds and synthetic environmental contaminants on the Proposition 65 list (both are also regulated as industrial substances).

**Figure 2**  
**Percentages of Listed Chemicals Covered by Federal Programs<sup>82</sup>**



<sup>82</sup> See legend for Figure 1, *supra*.

Approximately half of listed Proposition 65 carcinogens may not be suitable regulatory targets. At least 15% of listed carcinogens are no longer commercially used in the U.S.; this includes about half of the listed agricultural chemicals. An additional 30% of listed carcinogens have extremely limited potential for widespread human exposure because their use is restricted to medical or research settings. Listed drugs in particular are unlikely to be discharged to drinking water and are exempt from Proposition 65 warning requirements.

In spite of the inclusion of substantial proportions of irrelevant compounds, Proposition 65 has clearly extended regulatory controls to a larger absolute number of chemicals with the potential for widespread human exposure than any federal statute. Its discharge ban, for example, affects four times as many carcinogenic industrial substances than are regulated under the Clean Water Act. In addition, although significant proportions of listed industrial chemicals are covered by major federal environmental statutes, these programs rarely address exposures through consumer products, which are a principal focus of Proposition 65's warning requirements.<sup>83</sup>

### *Reproductive Toxicants*

One hundred and twenty-seven compounds are listed as developmental or reproductive toxicants under Proposition 65. Table 3 also classifies these compounds into broad categories of chemical use. In contrast to carcinogens, the Proposition 65 list of reproductive toxicants is dominated by one type of chemical use. The overwhelming majority (80%) of listed reproductive toxicants are therapeutic drugs.<sup>84</sup>

<sup>83</sup> Excellent examples are provided by methylene chloride and para-dichlorobenzene. While these chemicals are targeted by some federal regulatory programs, important efforts to reduce consumer exposures through paint strippers and air fresheners have been conducted using the warning requirements of Proposition 65. ATTORNEY GENERAL, PROPOSITION 65 LITIGATION SUMMARY (1991).

<sup>84</sup> Listed drugs can be further categorized into anti-neoplastics (20), antibiotics (16), hormones (13), benzodiazepine tranquilizers (7), anti-convulsant drugs (4) and

All other chemical use classes represent about 10% or less of the total list. Twelve percent are agricultural chemicals, 9% are industrial substances, 6% are food constituents (all chlorinated hydrocarbon environmental contaminants), 6% are associated with tobacco, alcohol or other drugs, and 3% are energy-related substances.

Figure 2 illustrates the percentage of listed reproductive toxicants that are covered by federal programs focused on controlling the quality of air, water, land or the workplace. Reproductive toxicants appear to be addressed even less frequently than carcinogens (Figure 2(a)), but this reflects the predominance of listed drugs, which are rarely covered by major environmental statutes (Figure 2(h)). Focusing on the chemical use classes that have been the target of conventional regulatory programs (Figure 2(b-e)), reproductive toxicants are generally addressed as frequently or more frequently than listed carcinogens. It is important to note that federal regulatory coverage rarely address exposures through consumer products, a principal focus of Proposition 65's warning requirements.<sup>85</sup>

The apparently extensive regulatory coverage is largely attributable to the small number of substances in widespread commercial use that have been identified as reproductive toxicants under Proposition 65. Just 12 chemicals with industrial uses have been listed. Several ubiquitous environmental contaminants (lead, mercury, PCBs, TCDD) have been historically important regulatory targets. Four other commercially significant chemicals (carbon disulfide, ethylene glycol monoethyl and monomethyl ether and toluene) have been addressed by most environmental statutes. Just 15 agricultural chemicals have been listed. Use of many of these pesticides has been virtually eliminated (e.g., aminopterin, cyhexatin, DBCP, dinoseb, hexachlorobenzene, kepone, warfarin).<sup>86</sup> Only a few are widely used (e.g., benomyl, dermatologic agents (2)).

<sup>85</sup> An excellent example is provided by lead. While the compound is targeted by all federal regulatory programs, important efforts to reduce consumer exposures through food, wine and ceramics have been conducted using the warning provisions of Proposition 65. ATTORNEY GENERAL, *supra* note 83.

bromoxynil, cyanazine, carbon disulfide, ethylene oxide).<sup>87</sup>

Most listed reproductive toxicants are not suitable regulatory targets for Proposition 65. The drugs which dominate the list are already subject to more stringent FDA regulation. While there is widespread exposure to a number of drugs,<sup>88</sup> usage is unlikely to be affected by Proposition 65's regulatory requirements.<sup>89</sup> Less than one-quarter of listed reproductive toxicants are appropriate targets for regulatory provisions aimed at eliminating drinking water contamination and reducing public exposure generally.

## Conclusions

### *The Tradeoffs of List-Based Regulation*

The size of the Proposition 65 list is itself an indication of the Act's capacity to reform the status quo of toxics regulation. By ensuring that all identified carcinogens and reproductive toxicants become subject to its provisions almost automatically, Proposition 65 has precluded the time-consuming, case-by-case debates which have plagued efforts to

<sup>86</sup> EPA, SUSPENDED, CANCELLED AND RESTRICTED PESTICIDES (1990).

<sup>87</sup> CALIFORNIA DEPARTMENT OF FOOD AND AGRICULTURE (CDFA), PESTICIDE USE REPORT ANNUAL 1988 (1990).

<sup>88</sup> A number of listed antibiotics (e.g., doxycycline and tetracycline), anti-convulsants (e.g., phenytoin) and benzodiazepines (e.g., librium and valium) are frequently prescribed, R. TALLARIDA, MPD 1985: MOST PRESCRIBED DRUGS 1985 (1985), perhaps at doses of reproductive concern. Friedman et al., *Potential Human Teratogenicity of Frequently Prescribed Drugs*, 75 OBSTET. GYNECOL. 594-599 (1990). Two listed drugs (aspirin and retinols) are available over the counter. Despite significant federal controls, there is widespread abuse of a number of listed drugs, both illegal (anabolic steroids, cocaine) and legal (alcohol, tobacco, toluene).

<sup>89</sup> Proposition 65's discharge ban is generally irrelevant for listed drugs. As currently implemented, Proposition 65's warning requirements for therapeutic drugs are less stringent and less informative than required federal warnings about reproductive toxicity. Pease, *supra* note 42. Proposition 65's most significant impact in regard to drugs has involved requiring warnings about the reproductive effects of alcohol and aspirin earlier than mandated federally. The law may also result in occupational warnings in pharmaceutical manufacturing that would not be required under existing federal laws.

extend the regulatory coverage of most federal laws. No other regulatory program is based on such a large list of potential targets or has established as many regulatory levels as quickly.<sup>90</sup> Virtually the entire spectrum of political participants in the Proposition 65 debate seem to agree that the Act has resulted in a far more rapid assessment of carcinogens and reproductive toxicants than has occurred under other state and federal legislation.<sup>91</sup>

The politically charged effort to create a list of regulatory targets inevitably involves significant tradeoffs between extending regulatory coverage, facilitating efficient regulation and ensuring scientific consistency. Proposition 65's approach to hazard identification was designed to correct the poor performance of traditional regulatory programs. Lists of Clean Water Act (CWA) priority pollutants and Clean Air Act (CAA) hazardous air pollutants, for example, are substantially shorter than the Proposition 65 list and clearly do not address all commercially significant identified hazards. While these federal lists exemplify substantial flaws in the existing hazard identification process,<sup>92</sup> they also reflect an effort to focus monitoring and control requirements on just those chemicals which are likely to be discharged into an environmental medium.

<sup>90</sup> Pease et al., *supra* note 79.

<sup>91</sup> Corash and Shapiro, *California's Proposition 65: An Isolated Experiment or a Troubling Precedent?* in CLEAN WATER AND TOXIC WASTE: AT WHAT COST FOR WHAT GAIN? (1989); W. NORTH, RISK ASSESSMENT UNDER PROPOSITION 65: A PERSPECTIVE FROM THE SCIENCE ADVISORY PANEL (1989) (proceedings of the 82nd Annual Meeting of the Air and Waste Management Association, Anaheim, CA); Roe, *Barking up the Right Tree: Recent Progress in Focusing the Toxics Issue*, 13 COL. J. ENVIRON. LAW 275-283 (1988).

<sup>92</sup> Under both federal statutes, the development of lists which specify targets for regulatory control has been incomplete and very time-consuming. The 126 priority pollutants which are the focus of CWA regulation represent only 25% of the most frequently occurring chemicals in wastewater from industries and publicly owned treatment works, but the list has not been modified since 1977. Slow progress with identifying hazardous air pollutants under the original Section 112 of the CAA recently stimulated Congress to legislatively expand its list of regulatory targets from 7 to 189 compounds. Robinson & Pease, *From Health-Based to Technology-Based Standards for Hazardous Air Pollutants*, 81 AM. J. PUB. HEALTH 1518-1523 (1991).

Compared with most environmental legislation, Proposition 65 strikes a different balance between extent of coverage and applicability of regulatory requirements. Rather than restrict its coverage to chemicals likely to be affected by its provisions, it adopts an inclusive approach to hazard identification. To avoid the political debates likely to accompany considerations of regulatory relevance, the law specifies that sufficient scientific evidence is the only appropriate criterion for selecting targets. As a consequence, about 45% of listed carcinogens and 75% of listed reproductive toxicants are not substantially affected by Proposition 65's warning requirements or discharge ban. This regulatory irrelevance can occur because a substance has already been banned (e.g., most listed pesticides), because it has no important commercial use (e.g., laboratory research chemicals), because its use is controlled by more stringent requirements (e.g., therapeutic drugs) or because its use cannot be affected by Proposition 65 requirements (e.g., illegal drugs).

The extent of administrative inefficiency introduced by this inclusive approach to hazard identification varies with the specific regulatory requirements of Proposition 65. Restricting the application of its discharge ban to chemicals likely to be released to drinking water would reduce monitoring requirements, facilitate permitting activity and simplify enforcement.<sup>93</sup> For Proposition 65's warning requirements, there is less of a need to focus on a short list of regulatory targets. The burden of providing warnings about exposures to listed chemicals is not assigned to an administrative agency but is instead spread among businesses which have better access to information about chemical use. While compliance with Proposition 65's warning requirements could be better assured if a regulatory agency monitored chemical exposures, the law provides significant incentives for businesses to police themselves.

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<sup>93</sup> As of January 1992, there had been no effort to enforce Proposition 65's discharge ban. Citizen suits have been hampered by the absence of monitoring data on most listed substances. A principal reason for this inaction is the substantial administrative resources required to extend the State's water quality permit system to so many new chemicals.

Important tradeoffs between coverage, efficiency and consistency have been obscured throughout the Proposition 65 listing debate as parties have appealed to science to justify their policy preferences. Environmentalists sought to increase the number of substances subject to preventive regulation by restricting listing decisions to scientific considerations: is there sufficient evidence of hazard? is there a scientific consensus that a substance is a hazard? The actual goal of this emphasis on science was not, however, to guarantee that listed substances shared consistent evidence, but rather to eliminate considerations of regulatory impact from the hazard identification phase of risk regulation. By combining hazard identifications conducted by different organizations without specifying a uniform threshold of sufficient evidence, Proposition 65 values extending regulatory coverage over ensuring scientific consistency. While this tradeoff has not had a major impact on listed carcinogens, it allowed the State to introduce a double standard for identifying developmental and reproductive toxicants. Substantial evidence of reproductive toxicity (including both human and animal data) has been required to list industrial substances, but much less evidence (including chemical similarity alone) has been accepted as sufficient for listing drugs.

Opponents of Proposition 65 have also maintained that “science [should] be given the preeminent role” in the implementation process.<sup>94</sup> The regulated community and the Deukmejian Administration sought to minimize the law’s regulatory impact by appealing to scientific considerations in order to delay hazard identification. “Sound science” justified shortening the list to cover only toxicants with human evidence and adopting substance-by-substance review procedures. As with environmentalists, the Administration’s emphasis on science obscured the political balance it wanted to strike between regulatory coverage, efficiency and consistency. To prevent the development of an extensive list of new regulatory targets, listing was

<sup>94</sup> Kizer et al., *Sound Science in the Implementation of Public Policy: A Case Report on California’s Proposition 65*, 260 JAMA 951-955 (1988).



focused on substances unlikely to be affected by Proposition 65's requirements and scientific concerns were emphasized at the expense of accelerated hazard identification.

*Recommendations to Improve the Proposition 65 Listing Process*

Although the Proposition 65 list of carcinogens and reproductive toxicants has now grown to include virtually all hazard identifications made by national and international organizations, the Act's mandate "to engage in a diligent, thorough, and continuing search for additional chemicals"<sup>95</sup> remains unfulfilled. Throughout the implementation of Proposition 65, the listing process has exhibited only a limited capacity to select chemicals for evaluation based on potential health risks or to evaluate chemicals not already identified as hazards by other organizations.

The failure to establish an effective system for assessing unaddressed toxic chemicals can be attributed to limitations in the Act's original statutory scheme as well as to the State's administrative implementation of the law. Proposition 65 itself does not mandate any procedure for selecting candidate toxicants for listing.<sup>96</sup> Its emphasis on scientific consensus helped shape a listing process that selects candidate chemicals based on sufficiency of evidence rather than on public health concerns.<sup>97</sup> To prevent the law from imposing new

<sup>95</sup> *AFL-CIO v. Deukmejian*, 212 Cal. App. 3d at 440.

<sup>96</sup> Earlier environmental policy proposals to prioritize chemicals for testing and toxicological evaluation by presence in drinking water or by volume of use (embodied legislatively in Lloyd Connelly's Assembly Bill 2582: The Pure Drinking Water and Safe Chemical Act of 1985) were not incorporated into the Proposition 65 initiative.

<sup>97</sup> Once the SAP completed its review of chemicals included on Proposition 65's "minimum" list of carcinogens, additional compounds were considered on the basis of extent of scientific evidence. Beginning with substances which had been classified by the EPA Carcinogen Assessment Group (4/22/88) and IARC (9/16/88), the SAP moved on to compounds identified by the NTP as having three or four positive animal studies (4/14/89) and then to those having two positive studies (4/6/90). The SAP's listing agenda for reproductive toxicants was initially determined by an

regulatory burdens on the business community, the Deukmejian Administration limited the listing agenda to known hazards and continually postponed prioritizing unassessed chemicals for evaluation by the SAP.<sup>98</sup>

informal agreement among members of the Reproductive Subpanel to focus on those substances with sufficient human evidence.

Efforts to address chemicals on the basis of public concern have been relatively limited. The most extensive effort to bring new chemicals before the SAP for consideration focused on pesticides. Concerned "about the shortness of the Prop 65 list in regard to carcinogenic and teratogenic pesticides," the National Farm Workers Health Group recommended 121 possibly carcinogenic and 66 possibly teratogenic pesticides for review to the CHWA. Letter from M. Moses to W. Kilgore, SAP Chair (July 14, 1988). Less than one-sixth of the carcinogens were subsequently evaluated by the SAP. Focusing on 18 pesticides and herbicides that EPA had designated as having sufficient evidence of carcinogenicity in animals, SAP, Dec. 16, 1988, the SAP considered several pesticides (e.g., lactofen) that were neither registered nor used in California. SAP, Dec. 16, 1988, at 42. Less than one-third of the teratogens were subsequently evaluated by the SAP.

<sup>98</sup> For carcinogens, no state resources have ever been devoted to prioritizing candidate chemicals for listing under Proposition 65.

The history of attempts to develop a prioritization scheme for reproductive toxicants is indicative of the state's efforts to control the listing process. The absence of established authoritative lists stimulated early interest in establishing priorities for SAP consideration, given the large universe of chemicals with at least some evidence of reproductive toxicity. At a meeting in April 1988, the SAP Reproductive Subpanel specified a list of 12 compounds as priorities for future consideration based on the extent of scientific data and the potential for human exposure. SAP Subpanel, April 14, 1988. To supplement the SAP effort, CDHS prepared a paper which prioritized compounds on the basis of available chemical emissions and use data. J. VANDENBERG et al., *THE USE OF AN EVALUATED TOXICITY DATA BASE IN SETTING PRIORITIES FOR ASSESSMENT OF REPRODUCTIVE TOXICANTS* (1989) (proceedings of the 82nd Annual Meeting of the Air and Waste Management Association, Anaheim, CA). The CHWA, however, ignored these schemes and insisted that other chemicals have a higher priority for listing consideration.

Maintaining that the SAP should focus on chemicals "with sufficient evidence of reproductive toxicity in people," memo from S. Book to H. Collins, CDHS (Jan. 11, 1990) (concerning prioritization of reproductive toxicants), the CHWA proceeded to focus SAP evaluations on drugs (e.g., 4 prescription antibiotics on the SAP's October 1989 agenda). When SAP member Diana Pettiti stated that "in looking over the list of potential reproductive toxicants that we are to consider here today, it doesn't sort of match with my notion of what are serious potential teratogens," SAP Chair Dorothy Burk explained that the Reproductive Subpanel "prioritized a number

Several recommendations can be made to improve future hazard identification efforts:

- The State should support the creation of an independent chemical review process that can make unique contributions to hazard identification. While the Proposition 65 listing methods which ensure that the law automatically covers hazards identified by other organizations have been implemented, the State has not fulfilled Proposition 65's mandate to conduct de novo hazard identification. There are two major sources of toxicological data on compounds that have not been assessed by other authoritative organizations

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of chemicals which, in our opinion, needed to be addressed. Some of the ones you see on here were not ones that we prioritized. They were put on by others." SAP, Oct. 20, 1989, at 33-34.

The SAP never regained control of its agenda. Only half of the compounds originally prioritized by the SAP have subsequently been evaluated and just 3 have been identified as reproductive toxicants. Consideration of the Reproductive Subpanel's number one priority (environmental tobacco smoke) has been continually postponed. (The other priority chemicals that have not yet been evaluated include: cadmium, arsenic, caffeine, styrene, xylene, benzene, thiouracils and anesthetic gases (nitrous oxide). SAP Subpanel, Feb. 22, 1989.)

After the SAP's sole expert on reproductive toxicity insisted that "the more important task before the Panel is the order of consideration of non-drug chemicals," CHWA essentially took over the listing process for reproductive toxicants, automatically listing FDA-rated drugs and proposing virtually no compounds for SAP review.

Recently, the CHWA has acknowledged that the current listing process for reproductive toxicants could be considered "arbitrary" and initiated the development of a "clear, predictable scheme to identify chemicals of concern." Memo from S. Book to H. Collins, CDHS (Jan. 11, 1990) (concerning prioritization of reproductive toxicants). CDHS developed an elaborate scheme for selecting chemicals for consideration on the basis of several different approaches, ranging from expert identification to cross-referencing available toxicity data with human exposure databases. Donald et al., *Prioritizing Candidate Reproductive/Developmental Toxicants for Evaluation*, REPROD. TOXICOL. (1991) (in press). As of January 1992, however, the State has not used the CDHS priority candidate list of 42 industrial and agricultural chemicals to revive the Proposition 65 listing process. While two priorities (PCBs and toluene) have been listed as a result of SAP evaluations that began before the scheme was proposed and one (ribavirin) has been listed as a result of FDA labeling requirements, none of the remaining chemicals have been placed on the SAP agenda for consideration.

which could be evaluated: public databases compiling bioassay results<sup>99</sup> and regulatory agency files containing premarket test results.<sup>100</sup>

- De novo hazard identification efforts should principally focus on evaluating reproductive toxicants for listing under Proposition 65. While existing federal programs have established a process to screen and test commercially significant compounds and to identify potential carcinogens, no such effort is currently focused on reproductive toxicants. Since new carcinogen identifications conducted by authoritative bodies are automatically incorporated into the Proposition 65 list, there are only a few remaining sources of carcinogenicity data requiring evaluation (e.g., pesticide test results). In contrast, there are significant opportunities to contribute to reproductive hazard identification since these toxicants are generally unaddressed by existing state and federal regulatory systems.<sup>101</sup>

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<sup>99</sup> The Carcinogen Potency Database, Gold et al., *Third Chronological Supplement to the Carcinogen Potency Database: Standardized Results of Animal Bioassays Published Through December 1986 and by the National Toxicology Program Through June 1987*, 84 ENVIRON. HEALTH PERSPECT. 215-285 (1990), compiles published bioassay results on potential carcinogens. The Registry of Toxic Effects of Chemical Substances and the Hazardous Substances Data Bank contain extensive summaries of reproductive toxicity test results.

<sup>100</sup> A considerable amount of unassessed data exists in the files of regulatory agencies. CalEPA's Department of Pesticide Regulation, for example, has assembled a large database which includes results from two-year carcinogenicity bioassays and reproductive toxicity studies on a variety of agricultural chemicals that have not been evaluated by authoritative organizations.

To date, California regulatory agencies have generally not sought to bring chemicals into the Proposition 65 listing process. CHWA attempts to solicit nominations of priority chemicals from agencies have identified only a few chemicals for SAP evaluation. Since the passage of Proposition 65, for example, CDFA nominated only one pesticide for listing as a carcinogen (captafol, SAP, Sept. 16, 1988) and three for listing as reproductive toxicants (cycloheximide, cyhexatin and dinoseb, SAP, Dec. 16, 1988).

<sup>101</sup> GAO, *supra* note 5.

- Chemicals selected as candidates for listing under Proposition 65 should be prioritized for evaluation on the basis of potential for significant human exposure and relevance of the regulatory control requirements of Proposition 65.<sup>102</sup> It is imperative to develop more effective selection methods than alphabetic order (previously used by the SAP with most IARC and NTP carcinogens) or anecdotal scientific judgment (used by the SAP with its initial list of reproductive toxicants). There are a number of sources of data on chemical use and exposure which have not generally been used to guide the selection of candidate chemicals.<sup>103</sup> Early assessment of whether a chemical is likely to be affected by Proposition 65's requirements can avoid wasting resources on listing irrelevant substances (e.g., illegal drugs).

- The SAP's institutional capacity to conduct independent hazard identification should be substantially strengthened. The SAP should be allowed control over its own agenda and provided with sufficient resources to carry on *de novo* chemical evaluations. Quarterly SAP meetings should be reinstituted to provide adequate time for data reviews. To facilitate Proposition 65's unique mandate to identify reproductive toxicants, the Subpanel on Reproductive Toxicity should be reestablished.

- The SAP should address science policy questions associated with the Proposition 65 listing process, but limit

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<sup>102</sup> Consistent with the State's effort to focus hazard identification efforts on substances already covered by regulation, the State's current fifteen top priorities for evaluation as reproductive toxicants, Donald et al., *supra* note 98, have already been listed as carcinogens under Proposition 65. Listing them as reproductive toxicants will have minimal regulatory impact, requiring only supplemental warning language. The State's existing priority list of reproductive toxicants should be modified to focus on substances that are not already covered by Proposition 65, unless regulatory levels based on reproductive effects are likely to be lower than those based on carcinogenicity.

<sup>103</sup> These include the EPA's Chemicals on Reporting Rules Database and CalEPA's pesticide use inventories. CDFA, *supra* note 87.

its consideration of risk assessment or regulatory policy issues. Listing decisions are the only statutorily mandated function of the Governor's "qualified experts" under Proposition 65. In the past, the Panel's attention has been diverted to other issues in order to delay the hazard identification process.<sup>104</sup>

One major outstanding hazard identification issue involves whether listing decisions should emphasize scientific or regulatory consistency. Is it more important to ensure that all listed substances are supported by consistent scientific evidence or to ensure that all substances covered by a Proposition 65 listing method are listed? With carcinogens, the State has subjected substances which could be identified on the basis of authoritative bodies or regulatory labeling requirements to a sufficiency of evidence test and refused to list many commercially significant compounds. With reproductive toxicants, the State has avoided evaluating supporting evidence and listed many irrelevant therapeutic compounds automatically because of FDA labeling requirements.

To encourage a more consistent approach to listing decisions, the SAP must explicitly address the issue of what constitutes sufficient evidence to justify preventive regulation under Proposition 65. The Panel can (a) reassert the relatively high standard of evidence represented by current SAP hazard identification criteria and insist that all procedurally-based listing decisions be subjected to a sufficiency of evidence test; or (b) revise its standards to accept that lesser amounts of evidence are sufficient to identify a substance as "known to the State" to cause cancer or reproductive toxicity. Substances with relatively limited

<sup>104</sup> As part of its strategy to limit de novo hazard identification, the Deukmejian Administration focused SAP meetings on reviewing Proposition 65 risk assessments rather than chemical data. cursory SAP reviews did not substantially modify the scientific content of most risk assessments, but they did monopolize the SAP agenda (on average, six 50 page documents were presented and discussed at each meeting after the fall of 1988). Cancer policy issues are more appropriately addressed within the process California has established to modify its Guidelines for Chemical Carcinogen Risk Assessment, relying on expert committees with substantially broader expertise than the Proposition 65 SAP.

evidence have been listed as a result of Proposition 65's procedural requirements.<sup>105</sup> The Panel must consider whether these listings have established a new minimum threshold of evidence that should be applied in future chemical evaluations. Given the preventive goals of Proposition 65, it may be appropriate to extend its scope beyond traditional "known" toxicants to suspect compounds with more limited evidence of hazard.<sup>106</sup>

Proposition 65 provides an interesting model for reforming hazard identification in environmental regulation. It has successfully increased the number of carcinogens and reproductive toxicants affected by regulatory requirements. Its dramatic extension of regulatory coverage has occurred at the expense of both regulatory relevance and scientific consistency. Moreover, political concerns about automatically expanding the scope of regulation have prevented a major effort to evaluate unassessed compounds. The State's failure to contribute many new hazard identifications does not reflect a scientific determination that all potential chemical carcinogens and reproductive hazards have been discovered, but is rather a consequence of the political importance of listing under Proposition 65. In the future, the challenge in implementing Proposition 65 will involve establishing an effective process for selecting and evaluating new compounds.



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<sup>105</sup> Some FDA-labeled therapeutic compounds have been identified as reproductive toxicants on the basis of membership in a chemical class, structure-activity relationships, limited bioassay results or epidemiological case reports.

<sup>106</sup> The SAP should consider how it will proceed with carcinogen identification after all chemicals with lifetime bioassay data have been reviewed. In particular, the SAP should decide whether it will adopt recent proposals to identify carcinogens on the basis of short-term test results alone. Ashby & Marrod, *Detection of Human Carcinogens*, 352 NATURE 185-186 (1991).